

C2  
B2  
(concluded)

prevention, and causing said human [mammal] to inhale a therapeutically-effective amount of a nitric oxide-releasing compound.

B3

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33. (Amended)

The method of claim <sup>7</sup>31, wherein said

compound is selected from the group consisting of S-nitroso-N-acetylpenicillamine, S-nitrosocysteine, [nitroprusside,] nitrosoguanidine, glyceryl trinitrate, isoamyl nitrite, inorganic nitrite, azide, and hydroxylamine.

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38. (Amended)

The method of claim 31, wherein said

inhalation step is preceded by a step comprising causing said human [mammal] to inhale a therapeutically-effective amount of gaseous nitric oxide.

C4  
B5

44. (Amended)

A method of improving gas exchange in

the lungs of a mammal, said method comprising identifying a mammal in need of said improved gas exchange, and causing said mammal to inhale a therapeutically-effective amount of a nitric oxide-releasing compound.

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46. (Amended)

The method of claim <sup>14</sup>44, wherein said

nitric oxide-releasing compound is selected from a group consisting of S-nitroso-N-acetylpenicillamine, S-nitrosocysteine, nitroprusside, nitrosoguanidine, glyceryl trinitrate, isoamyl nitrite, inorganic nitrite, azide, and [or] hydroxylamine.

(C)

B6  
S15  
47. (Amended) A method of delivering a pharmacoactive compound into the lungs of a mammal, said method comprising causing said mammal to inhale said compound in the form of a liquid or solid suspended in a gas comprising a therapeutically-effective amount of nitric oxide.

B7  
29 48. (Amended) A device comprising  
a vessel containing a nitric oxide-donor compound  
effective for treating bronchoconstriction or reversible pulmonary vasoconstriction, said compound being suspended in a pressurized or liquified propellant gas;  
a housing defining (a) a port onto which said vessel is mounted and (b) a lumen in communication with said port; and  
a mechanism for controllably releasing said propellant from said vessel into said lumen, thereby releasing said suspended compound from said vessel into said lumen;  
said lumen being configured to route a therapeutically effective amount of said compound suspended in said released propellant into the respiratory system of a person.

B8  
29 29. (Amended) The device of claim 29, wherein said compound is selected from a group consisting of S-nitroso-N-acetylpenicillamine, S-nitrosocysteine, [nitroprusside,] nitrosoguanidine, [glyceryl trinitrate,] isoamyl nitrite, inorganic nitrite, azide, and [or] hydroxylamine.

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33 75. (Amended) A device comprising  
a vessel containing a pressurized or liquified  
propellant gas;

B8  
(concluded)  
a housing defining (a) a chamber containing a nitric  
oxide-donor compound effective for treating bronchoconstriction  
or reversible pulmonary vasoconstriction, and (b) a lumen in  
communication with said chamber;

a mechanism for controllably releasing said gas from  
said vessel into said chamber, thereby suspending said compound  
in said gas;  
said lumen being configured to route a therapeutically effective  
amount of said compound into the respiratory system of a person.

B9  
35 75. (Amended) The device of claim 33, wherein said  
nitric oxide-donor compound is selected from a group consisting  
of S-nitroso-N-acetylpenicillamine, S-nitrosocysteine,  
[nitroprusside,] nitrosoguanidine, [glyceryl trinitrate,] isoamyl  
nitrite, inorganic nitrite, azide, and [or] hydroxylamine.

Add the following new claims 76-134:

Sub 88  
B10  
-- 76. An apparatus for introducing NO gas into the  
respiratory system of a mammal, comprising  
a source of pressurized NO-containing gas;  
a source of pressurized O<sub>2</sub>-containing gas;  
a gas blender;

means for controllably releasing said gases from said sources into said blender, thereby forming a gas mixture which continuously flows out of said blender; and

a tube having a lumen in communication with said blender, said tube being configured to route said gas mixture into the respiratory system of a mammal. --

-- 77. The apparatus of claim 76, wherein said tube comprises a nitrogen dioxide ( $\text{NO}_2$ ) scavenger. --

37 -- 78. The apparatus of claim 76, wherein said tube comprises an  $\text{NO}_2$  analyzer. --

38 -- 79. The apparatus of claim 76, wherein said NO in said source of pressurized NO is diluted in an inert gas. --

39 -- 80. The apparatus of claim 79, wherein said inert gas is  $\text{N}_2$ . --

40 -- 81. The apparatus of claim 76, wherein said  $\text{O}_2$ -containing gas is 100%  $\text{O}_2$ . --

41 -- 82. The apparatus of claim 76, wherein said tube comprises a mask configured to route said gas mixture into the respiratory system of a mammal. --

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Sub  
C6P 10  
(continued)

-- 83. An apparatus for introducing NO gas into the respiratory system of a mammal, comprising  
sources of pressurized NO gas, N<sub>2</sub> gas and O<sub>2</sub> gas;  
a gas reservoir;  
means for controllably releasing said gases into said gas reservoir, thereby forming a gas mixture within said reservoir; and  
a tube having a lumen in communication with said reservoir, said tube being equipped with a flowmeter, wherein said tube is configured to route said gas mixture into the respiratory system of a mammal;  
provided that the setting on said flowmeter is such that the residence half time of NO in said reservoir during use by said mammal is 15 seconds or less. --

43 -- 84. The apparatus of claim 83, wherein said tube comprises an NO<sub>2</sub> scavenger. --

44 -- 85. The apparatus of claim 83, wherein said tube comprises an NO<sub>2</sub> analyzer. --

45 -- 86. The apparatus of claim 83, wherein said tube comprises a mask configured to route said gas mixture into the respiratory system of a mammal. --

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C7

-- 87. An apparatus for introducing NO gas into the respiratory system of a patient, comprising:  
a source of pressurized NO gas;  
an enclosure suitable for providing an ambient atmosphere from which said patient can inhale;  
means for charging said atmosphere with NO from said source; and  
means for causing said atmosphere to have a high gas turnover rate.

B10  
(continued)

47 -- 88. The apparatus of claim 46, wherein said NO in said source of pressurized NO is diluted in an inert gas. --

48 -- 89. The apparatus of claim 47, wherein said inert gas is N<sub>2</sub>. --

49 -- 90. The apparatus of claim 47, wherein said enclosure is a mask. --

50 -- 91. The apparatus of claim 47, wherein said enclosure is a tent. --

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D11

-- 92. An apparatus for introducing NO gas into the respiratory system of a patient, comprising:  
a source of pressurized NO gas;

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a ventilator comprising a ventilation circuit; and means for controllably releasing said gas into said ventilation circuit. --

-- 93. The apparatus of claim 92, wherein said ventilation circuit comprises an NO<sub>2</sub> scavenger. --

-- 94. The apparatus of claim 92, wherein said ventilation circuit comprises an NO<sub>2</sub> analyzer. --

53 -- 95. The apparatus of claim 51, wherein said NO in said source of pressurized NO is diluted in an inert gas. --

54 -- 96. The apparatus of claim 53, wherein said inert gas is N<sub>2</sub>. --

Sub C9  
-- 97. An apparatus for introducing NO gas into the respiratory system of a mammal, comprising:  
a source of pressurized NO gas;  
a source of pressurized O<sub>2</sub>-containing gas;  
a housing equipped with a flowmeter; and  
means for controllably releasing said gases from said sources into said housing to form a gas mixture;  
said housing being configured to route said gas mixture into the respiratory system of said mammal. --

-- 98. The apparatus of claim 97, wherein said housing comprises an NO<sub>2</sub> scavenger. --

56 -- 99. The apparatus of claim 97, wherein said housing comprises an NO<sub>2</sub> analyzer. --

57 -- 100. The apparatus of claim 97, wherein said NO in said source of pressurized NO is diluted in an inert gas. --

58 -- 101. The apparatus of claim 100, wherein said inert gas is N<sub>2</sub>. --

59 -- 102. The apparatus of claim 97, wherein said O<sub>2</sub>-containing gas is 100% O<sub>2</sub>. --

60 -- 103. The apparatus of claim 97, wherein said housing comprises a mask configured to route said gas mixture into the respiratory system of a mammal. --

Sub 110  
-- 104. A method for treating or preventing reversible pulmonary vasoconstriction in a mammal, which method comprises providing an oxygen-containing gas mixture comprising NO at a therapeutically-effective concentration, and causing a mammal in need of said treatment to inhale a therapeutically-effective amount of said mixture, provided that the NO<sub>2</sub> concentration in said gas mixture is less than 12 ppm. --



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-- 105. The method of claim 104, wherein said gas mixture contains less than 1 ppm NO<sub>2</sub> when inhaled by said mammal. --

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-- 106. The method of claim 104, comprising the additional step of monitoring the concentration of NO<sub>2</sub> in said gas mixture, prior to said inhalation step. --

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(continued)

-- 107. The method of claim 104, comprising the additional step of passing said gas mixture through a NO<sub>2</sub> scavenger prior to said inhalation step. --

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-- 108. The method of claim 104, wherein said pulmonary vasoconstriction is acute pulmonary vasoconstriction. --

Sub  
C11

-- 109. The method of claim 104, wherein said mammal has or is at risk of developing a clinical condition selected from the group consisting of pneumonia, traumatic injury, aspiration or inhalation injury, fat embolism in the lung, acidosis, inflammation of the lung, adult respiratory distress syndrome, acute mountain sickness, post cardiac surgery acute pulmonary hypertension, persistent pulmonary hypertension of the newborn, perinatal aspiration syndrome, hyaline membrane disease, acute pulmonary thromboembolism, acute pulmonary edema, heparin-protamine reactions, sepsis, hypoxia, asthma, and status asthmaticus.

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cancel

-- 110. A method for treating or preventing reversible pulmonary vasoconstriction in a mammal, which method comprises providing an oxygen-containing gas mixture comprising NO at a therapeutically-effective concentration; monitoring the concentration of NO<sub>2</sub> in said gas mixture; and causing a mammal in need of said treatment to inhale a therapeutically-effective amount of said gas mixture. --

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Sub (continued)  
D16

-- 111. The method of claim 110, wherein said gas mixture contains less than 1 ppm NO<sub>2</sub> when inhaled by said mammal. --

-- 112. The method of claim 110, comprising the additional step of passing said gas mixture through a NO<sub>2</sub> scavenger prior to said inhalation step. --

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-- ~~113~~<sup>b8</sup>. The method of claim ~~110~~<sup>b8</sup>, wherein said pulmonary vasoconstriction is acute pulmonary vasoconstriction. --

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-- 114. The method of claim 110, wherein said mammal has or is at risk of developing a clinical condition selected from the group consisting of pneumonia, traumatic injury, aspiration or inhalation injury, fat embolism in the lung, acidosis, inflammation of the lung, adult respiratory distress

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syndrome, acute mountain sickness, post cardiac surgery acute pulmonary hypertension, persistent pulmonary hypertension of the newborn, perinatal aspiration syndrome, hyaline membrane disease, acute pulmonary thromboembolism, acute pulmonary edema, heparin-protamine reactions, sepsis, hypoxia, asthma, and status asthmaticus.

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(continued)  
-- 115. A method for treating or preventing reversible pulmonary vasoconstriction in a mammal, which method comprises providing an oxygen-containing gas mixture comprising NO at a therapeutically-effective concentration; scavenging NO<sub>2</sub> from said gas mixture; and after said scavenging step, causing a mammal in need of said treatment to inhale a therapeutically-effective amount of said resulting gas mixture. --

-- 116. The method of claim 115, wherein said gas mixture contains less than 1 ppm NO<sub>2</sub> when inhaled by said mammal. --

Sub D17  
-- 117. The method of claim 115, comprising the additional step of monitoring the concentration of NO<sub>2</sub> in said gas mixture, prior to said inhalation step. --

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77 -- 118. The method of claim 115, wherein said pulmonary vasoconstriction is acute pulmonary vasoconstriction. --

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P 10  
(continued)

-- 119. The method of claim 115, wherein said mammal has or is at risk of developing a clinical condition selected from the group consisting of pneumonia, traumatic injury, aspiration or inhalation injury, fat embolism in the lung, acidosis, inflammation of the lung, adult respiratory distress syndrome, acute mountain sickness, post cardiac surgery acute pulmonary hypertension, persistent pulmonary hypertension of the newborn, perinatal aspiration syndrome, hyaline membrane disease, acute pulmonary thromboembolism, acute pulmonary edema, heparin-protamine reactions, sepsis, hypoxia, asthma, and status asthmaticus.

-- 120. A method for treating or preventing bronchoconstriction in a mammal, which method comprises providing an oxygen-containing gas mixture comprising NO at a therapeutically-effective concentration, and causing a mammal in need of said treatment to inhale a therapeutically-effective amount of said mixture, provided that the NO<sub>2</sub> concentration in said gas mixture is less than 12 ppm. --

-- 121. The method of claim 120, wherein said gas mixture contains less than 1 ppm NO<sub>2</sub> when inhaled by said mammal. --

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-- 122. The method of claim 120, comprising the additional step of monitoring the concentration of NO<sub>2</sub> in said gas mixture, prior to said inhalation step. --

-- 123. The method of claim 120, comprising the additional step of passing said gas mixture through a NO<sub>2</sub> scavenger prior to said inhalation step. --

Sub C14  
B 10  
(continued)

-- 124. A method for treating or preventing bronchoconstriction in a mammal, which method comprises providing an oxygen-containing gas mixture comprising NO at a therapeutically-effective concentration; monitoring the concentration of NO<sub>2</sub> in said gas mixture; and causing a mammal in need of said treatment to inhale a therapeutically-effective amount of said gas mixture. --

-- 125. The method of claim 124, wherein said gas mixture contains less than 1 ppm NO<sub>2</sub> when inhaled by said mammal. --

Sub 21  
-- 126. The method of claim 124, comprising the additional step of passing said gas mixture through a NO<sub>2</sub> scavenger prior to said inhalation step. --

Sub C15  
-- 127. A method for treating or preventing bronchoconstriction in a mammal, which method comprises providing an oxygen-containing gas mixture comprising NO at a therapeutically-effective concentration; scavenging NO<sub>2</sub> from said gas mixture; and

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after said scavenging step, causing a mammal in need of said treatment to inhale a therapeutically-effective amount of said resulting gas mixture. --

-- 128. The method of claim 127, wherein said gas mixture contains less than 1 ppm NO<sub>2</sub> when inhaled by said mammal. --

Subp 23

-- 129. The method of claim 127, comprising the additional step of monitoring the concentration of NO<sub>2</sub> in said gas mixture, prior to said inhalation step. --

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(concluded)

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-- 130. The method of claim 104, wherein said mammal is a human. --

-- 131. The method of claim 110, wherein said mammal is a human. --

-- 132. The method of claim 115, wherein said mammal is a human. --

-- 133. The method of claim 120, wherein said mammal is a human. --

-- 134. The method of claim 124, wherein said mammal is a human. --